

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
2 October 2003 (02.10.2003)

PCT

(10) International Publication Number  
**WO 03/080574 A1**

(51) International Patent Classification<sup>7</sup>: C07D 211/58,  
451/04, 401/12, 403/12, A61K 31/4468, 31/46, A61P  
29/00, 31/12

SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US,  
UZ, VC, VN, YU, ZA, ZM, ZW.

(21) International Application Number: PCT/SE03/00480

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW);  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,  
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,  
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(22) International Filing Date: 24 March 2003 (24.03.2003)

(25) Filing Language: English

**Declarations under Rule 4.17:**

(26) Publication Language: English

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(i)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*

(30) Priority Data:  
0200919-9 25 March 2002 (25.03.2002) SE

— *of inventorship (Rule 4.17(iv)) for US only*

(71) Applicant (*for all designated States except US*): ASTRAZENECA AB [SE/SE]; S-151 85 Södertälje (SE).

**Published:**

(72) Inventor; and  
(75) Inventor/Applicant (*for US only*): CUMMING, John  
[GB/GB]; AstraZeneca R & D Alderley, Alderley Park,  
Macclesfield, Cheshire SK10 4TG (GB).

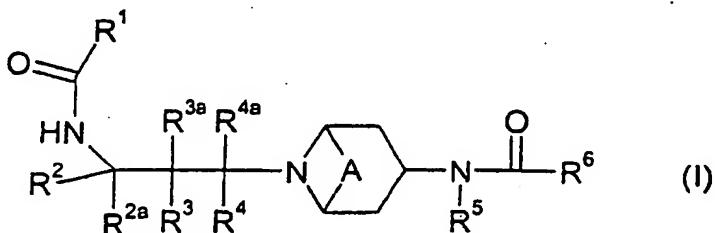
— *with international search report*

(74) Agent: GLOBAL INTELLECTUAL PROPERTY; AstraZeneca AB, S-151 85 Södertälje (SE).

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD,

(54) Title: PIPERIDINE OR 8-AZA-BICYCLO[3.2.1]OCT-3-YL DERIVATIVES USEFUL AS MODULATORS OF CHEMOKINE RECEPTOR ACTIVITY (ESPECIALLY CCR5)



(57) Abstract: The invention provides a compound of formula (I) wherein A, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>3a</sup>, R<sup>4</sup>, R<sup>4a</sup>, R<sup>5</sup>, and R<sup>6</sup> are as defined; or a pharmaceutically acceptable salt thereof or a solvate thereof; compositions containing these compounds, processes for preparing them and their use as modulators of chemokine activity (for example CCR5 activity).

WO 03/080574 A1

BEST AVAILABLE COPY

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 03/00480

## A. CLASSIFICATION OF SUBJECT MATTER

IPC7: C07D 211/58, C07D 451/04, C07D 401/12, C07D 403/12, A61K 31/4468,  
 A61K 31/46, A61P 29/00, A61P 31/12  
 According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: C07D, A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE, DK, FI, NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-INTERNAL, WPI DATA, PAJ, CHEM. ABS DATA

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 02070479 A1 (ASTRAZENECA AB), 12 Sept 2002 (12.09.02), page 9 - page 10, Table I, nos. 4-7, 28, the claims  --	1-13
P, X	WO 02076948 A1 (ASTRAZENECA AB), 3 October 2002 (03.10.02)  --	1-13
X	EP 1013276 A1 (PFIZER INC.), 28 June 2000 (28.06.00), the claims, the examples  --	1-13
X	WO 0187839 A1 (ASTRAZENECA AB), 22 November 2001 (22.11.01), page 32 - page 35, nos. 1, 54, 55, the claims  --	1-13

 Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:	
"A"	document defining the general state of the art which is not considered to be of particular relevance
"E"	earlier application or patent but published on or after the international filing date
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O"	document referring to an oral disclosure, use, exhibition or other means
"P"	document published prior to the international filing date but later than the priority date claimed
"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X"	document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y"	document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&"	document member of the same patent family

Date of the actual completion of the international search

23 May 2003

Date of mailing of the international search report

10-06-2003

Name and mailing address of the ISA/  
 Swedish Patent Office  
 Box 5055, S-102 42 STOCKHOLM  
 Facsimile No. + 46 8 666 02 86

Authorized officer  
**BEST AVAILABLE COPY**  
 Gerd Strandell/BS  
 Telephone No. + 46 8 782 25 00

## INTERNATIONAL SEARCH REPORT

International application No. PCT/SE 03/00480
--

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 0114333 A1 (ASTRAZENECA UK LIMITED), 1 March 2001 (01.03.01) --	1-13
X	WO 0076513 A1 (MERCK & CO., INC.), 21 December 2000 (21.12.00) --	1-13
X	WO 0190106 A2 (PFIZER LIMITED), 29 November 2001 (29.11.01) -- -----	1-13

BEST AVAILABLE COPY

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/SE03/00480

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 1-3  
because they relate to subject matter not required to be searched by this Authority, namely:  
**see next sheet**
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.  
PCT/SE03/00480

Claim 13 relates to methods of treatment of the human or animal body by surgery or by therapy or diagnostic methods practised on the human or animal body (Rule 39.1(iv)). Nevertheless, a search has been executed for this claim. The search has been based on the alleged effects of the compounds or compositions. These alleged effects must be well defined diseases or conditions. The expression "a chemokine mediated disease state" may relate to a number of different disorders and conditions, which can not be clearly defined by this expression. Thus, the search has mainly been restricted to the diseases mentioned in the description on pages 14 to 17.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

29/04/03

International application No.

PCT/SE 03/00480

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 02070479 A1	12/09/02		AU 2382102 A GB 0105077 D GB 0115579 D SE 0103797 D	01/07/02 00/00/00 00/00/00 00/00/00
WO 02076948 A1	03/10/02		GB 0107228 D	00/00/00
EP 1013276 A1	28/06/00		AP 200102186 D AP 200102187 D AU 1290400 A AU 1675100 A BG 105709 A BG 105721 A BR 9905977 A BR 9916585 A BR 9917007 A CA 2350073 A CA 2350573 A CN 1331591 T CN 1331691 T EE 200100344 A EE 200100345 A EP 1140085 A EP 1140920 A GB 9828420 D HR 20010478 A HU 0104795 A HU 0104910 A IL 143510 D IL 143512 D JP 2000212159 A JP 2002533393 T JP 2002533461 T NO 20013149 A NO 20013183 A PL 349091 A PL 349495 A TR 200101793 T TR 200101867 T TR 200200938 T WO 0038680 A WO 0039125 A GB 9922702 D	00/00/00 00/00/00 31/07/00 31/07/00 28/02/02 28/02/02 14/01/03 16/10/01 30/10/01 06/07/00 06/07/00 16/01/02 16/01/02 15/10/02 16/12/02 10/10/01 10/10/01 00/00/00 30/06/02 29/04/02 28/10/02 00/00/00 00/00/00 02/08/00 08/10/02 08/10/02 23/08/01 08/08/01 01/07/02 29/07/02 00/00/00 00/00/00 00/00/00 06/07/00 06/07/00 00/00/00
WO 0187839 A1	22/11/01		AU 5898101 A BR 0110767 A EP 1289957 A GB 0011838 D NO 20025430 A	26/11/01 11/02/03 12/03/03 00/00/00 18/12/02
WO 0114333 A1	01/03/01		AU 6461600 A EP 1212299 A JP 2003507456 T SE 9902987 D	19/03/01 12/06/02 25/02/03 00/00/00

BEST AVAILABLE COPY

## INTERNATIONAL SEARCH REPORT

Information on patent family members

29/04/03

International application No.

PCT/SE 03/00480

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 0076513 A1	21/12/00	AU	5473800 A	02/01/01
		US	6506777 B	14/01/03
WO 0190106 A2	29/11/01	AU	5248201 A	03/12/01
		EP	1284974 A	26/02/03
		GB	0014046 D	00/00/00
		NO	20025227 A	31/10/02
		US	2002013337 A	31/01/02
		GB	0015835 D	00/00/00

**BEST AVAILABLE COPY**